English translation of DE 100 13 093.3

Device for the controlled inhalation of therapeutical aerosols

The present invention relates to a device and a method for the controlled inhalation of therapeutical aerosols and in particular for the individual dosimetry of inhalable aerosols.

In the inhalation of drugs in form of aerosols, several factors are of importance for the deposition of the active ingredient in the lung. The deposition of the active ingredient in the lung depends on the particle properties of the active ingredient to be inhaled, such as the particle size, electric charge and hygroscopicity, the inhalation velocity (i.e. respiratory flow) of the patient and the inhalation depth (i.e. tidal volume) of a breath of the patient to be treated.

In various drugs which are to be inhaled in form of aerosols, the amount of inhaled active ingredient has to be given in extremely accurate doses since any overdosage could be critical to the patient. In case of conventional inhalation methods, the particle size is adapted to the drug to be administered. However, the patient's breathing pattern is not controlled in any way so that the individual dosage may vary strongly. In case of weak breathing (shallow, rapid respiration), the inhaled drug falls short of the recommended dose, whereas heavy breathing (deep, slow respiration) results in an overdosage.

EP-B-0 487 380 describes a drug delivery arrangement that recognizes an inhalation and administers the drug only during an inhalation phase of the breathing cycle while the patient is free to breathe as he likes. This freedom, however, varies from patient to patient, so that the dosages vary considerably. EP-A-0 965 355 describes a controlled inhalator with a predetermined aerosol volume and a limitation of the respiratory flow. In this inhalator, the respiratory flow and the tidal volume are adjusted within certain limits. However, as a mass product, this inhalator cannot be adapted to the concrete requirements as to the pulmonary function of a

specific individual. The parameters adjusted for the tidal volume and the respiratory flow are acceptable for the majority of patients, however, the drug administration for the individual patient is not optimal.

Therefore, the following problems occur in practice:

1. Many very obstructive patients are no longer capable of developing the necessary respiratory flow which they would, however, have to develop for an optimal aerosol application;

2. Many of these patients have only very restricted tidal volumes, above all patients with pulmonary emphysema or patients with very small lung volumes;

3. Every patient inhales at a different rate and with a different volume so that the drug dosage within the lung varies widely.

It is the object of the present invention to provide an improved device for a controlled inhalation of therapeutical aerosols. This object is achieved by the features of the independent claims.

The present invention is based on the idea to provide an inhalation device with means offering individual patient parameters and/or aerosol parameters for the inhalation as well as means that adapt the dosage of the aerosol/s as a function of the predetermined individual patient and/or aerosol parameters. Thus, the inhalation device according to the invention may be individually adapted to the patient's capabilities.

According to a first embodiment, the individual parameters are provided on a memory medium, for example on memory media that are available under the designations SmartCard, FlashCard or SmartLabel. The individual parameters are stored in the memory medium for example upon a measurement of the current pulmonary function of the patient (carried out e.g. by the family doctor). According to a first embodiment, the patient then inserts this medium (at home) into the

inhalation device, whereupon the individual data are read out. Alternatively, the memory medium is inserted into a separate device from which the individual parameters are transferred to the inhalation device. According to a further alternative embodiment, a modem is provided so that the inhalation device is provided with the individual parameters by the physician or the institution in charge via a data link (for example a telephone line).

According to a further embodiment, means for the manual data input of individual parameters are provided, e.g. by the respective keys. Alternatively, in the device according to the invention, the individual parameters are adjusted via manual control units, e.g. potentiometers, or manual switches.

Thus, the individual patient and/or aerosol parameters influence the individual dosage of the aerosol/s either manually or automatically (e.g. via a respective valve control). Since the amount of aerosol deposition in certain lung sections dependent on the particle size of the active ingredient, the tidal volume and the respiratory flow is known, the aerosol deposition in the lung can essentially be predetermined according to the present invention. The patient considers the adjusted breathing manoeuvre agreeable since it is adapted to his/her capabilities.

In a preferred embodiment, each breathing manoeuvre carried out by the patient is stored on the memory medium of the inhalation device so that the administration may be controlled after a certain period of therapy.

In a further preferred embodiment, the memory medium is re-programmable in order to provide adapted parameters for the correct breathing manoeuvre if the pulmonary function of the patient changes.

Preferably, the inhalation device according to the present invention prevents an overdosage, for example by pre-setting an action period or an action blockage, e.g. on the memory medium. This prevents the activation of the inhalation device by the patient as long as the necessary period of time between two successive inhalations has not lapsed. Preferably, the memory medium also serves for recording errors. It

records for example whether the atomiser pressure deviates too much from a desired range or whether the required atomiser pressure could not be built up at all. Moreover, the memory medium preferably records a possible safety cutoff when the pressure at the mouthpiece (positive pressure respiration) gets too high. In a further preferred embodiment, a too high deviation of the flow (either the atomiser flow of the aerosol or the auxiliary flow of the additional air supplied to the aerosol air or the sum of both flows) is recorded or an error message if one of the aforementioned flows for the inhalation could not be built up. Preferably, a termination of the inhalation is also recorded by the patient.

Preferably, the designation of the drug to be inhaled is also stored on the memory medium.

Moreover, according to a preferred embodiment, an access control for servicing is provided. Servicing software in the inhalation device for is activated by means of a specific code in the memory medium.

The inhalation device according to the invention offers the following advantages:

1. For each patient, an individually agreeable and optimal inhalation manoeuvre is adjusted or pre-set;

2. By pre-setting individual parameters, different substances may be applied to different desired areas of the lung;

3. The release of the active ingredient is made more reproducible;

4. The optimal dose of the active ingredient is applied to the desired section of the patient's lung.

5. By programming different breathing manoeuvres, different drugs may be inhaled with one device optimally and individually adapted for each patient;

6. The inhalation device according to the invention may immediately be updated to new substances, new breathing manoeuvres and changed respiratory flows;

7. In a memory medium, such as a SmartCard, breathing manoeuvres in the course of a therapy may be recorded and subsequently evaluated;

8. If the patient's pulmonary function changes, the inhalation device may easily be re-set to the changed basic condition;

9. The use of a propellant is not absolutely necessary.

According to the invention, all medicinal agents may be used which become effective either topically in the respiratory system or systemically. Suitable medicinal agents are analgesics, anti-angina agents, anti-allergic agents, antihistamines and anti-inflammatory agents, expectorants, antitussives, bronchodilators, diuretics, anticholinergics, corticoids, xanthines, oncotherapeutical agents as well as therapeutically active proteins or peptides, such as insulin and interferon.

The administration of medicinal agents for treating respiratory diseases, such as asthma, as well as prophylactics and agents for treating the mucosae of the tracheobronchial system is preferred. The administration of esters of retinol and vitamin A as described in EP-A-0 352 412 is particularly preferred. The medicinal agents may be in their free form or in form of a pharmaceutically acceptable salt or ester. A further possibility consists in embedding the medicinal agent in liposomes.

The medicinal agents may be packaged with conventional, pharmaceutically acceptable excipients.